SOAR Research – Faculty Proposal – Summer, 2016

Synthesis of Rhodium-DNA Model Complexes

Faculty: Stephen Dunham, Ph.D., Associate Professor of Chemistry

Student: Austin Mates

Project Start Date: May 31, 2016
Length of Project: 10 weeks

Description of the project
Synthesis of Rhodium-DNA Model Complexes

Dirhodium complexes consist of a pair of rhodium (Rh) atoms that are typically bridged by 1-4 small molecules (i.e. acetates or amidates).[1] Several dirhodium complexes have been identified for their ability to kill cells suggesting that these compounds could be used as chemotherapy agents. Over the past few years, we have prepared several dirhodium compounds and studied their binding with large pieces of DNA.[1] Because these DNA molecules contain thousands of atoms, there are many details of the Rh-DNA bonding and structure that are unknown. In order to better understand structures formed between dirhodium complexes and DNA, we will prepare and characterize model compounds with much smaller pieces of DNA.[2] By determining the structures of these smaller Rh-DNA model compounds, we may gain insights to how Rh is bound to larger pieces of DNA, and potentially how Rh-DNA adducts may kill cancer cells.

Synthesis and Isolation of Rhodium Complexes
The Rh compounds needed for this project are not available for purchase from any vendor. An initial goal of the project is synthesize and isolate several known dirhodium complexes.

Reactions with DNA model compounds
Our next experimental goal will be to react purified dirhodium complexes with individual DNA bases (dN, N=A, T, G, C) and small oligonucleotides (dNpN). We will isolate the Rh-DNA products from unreacted molecules by using high performance liquid chromatography (HPLC) and determine molecular structures of purified Rh-DNA model complexes by using nuclear magnetic resonance (NMR) and mass (MS) spectrometry.

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[1] S.U. Dunham, T.S. Remaley, B.S. Moore, D.L. Evans and S.U. Dunham, "Isolation, Characterization, and DNA Binding Kinetics of Three Dirhodium(II,II) Carboxyamidate Complexes: $Rh_2(\mu\text{-}L)(HNOCCF_3)_3$ where L= $[OOCCH_3]^-$, $[OOCCF_3]^-$, $[HNOCCF_3]^-$", *Inorganic Chemistry*, **50**, pp 3458-3463 (2011).
[2] K.M. Bartulovich, "Characterization of Two Orientational Isomers of a DNA-binding Dirhodium Compound", Moravian College, Honors Thesis in Biochemistry, May 2015.

Roles and responsibilities

- The project director, Stephen Dunham, will train Austin in methods for synthesizing dirhodium compounds, carrying out nucleic acid reactions, the use of instrumentation, and data analysis.
- Austin will prepare and present his findings during daily research meetings (~30-60 min).
- Austin will maintain a research laboratory notebook that will include regular and complete entries. Keeping a comprehensive laboratory notebook is a fundamental part of doing research in chemistry. The notebook will have an updated table of contents at the beginning. Daily entries will be clearly written and organized with experimental details, clear references to location and organization of electronic data, and a summary of results from each experiment. Prof. Dunham will look at Austin's notebook weekly throughout the summer and provide informal feedback. The notebook will be submitted to the Prof. Dunham upon completion of SOAR.
- Throughout the summer, Austin will prepare summary figures that clearly illustrate the results of key experiments. These summary figures will form the basis for poster or research talks about his SOAR experience.
- Austin may consider continuing this research as an independent study during the 2015-2016 academic year, so a final report/poster may not be required at the end of the summer but instead by the end of his research experience and in time for the Annual Student Scholarship and Creative Endeavors Day in Spring of 2017.

Project Timetable

- Weeks 1-3: Setup dirhodium synthesis reactions and learn to operate various instruments: HPLC for compound isolation, NMR, and MALDI-MS for rhodium compound characterization.
- Weeks 4-10: Carry out Rh-DNA model reactions with purified rhodium compounds and small nucleic acid compounds. Reactions will be monitored by HPLC, and products characterized by NMR and MALDI-MS.

Summary of benefits

Student engagement in discipline-appropriate scholarly research. Austin will be engaged in bioinorganic chemistry research that includes reading and summarizing primary literature, planning and performing experiments that require the use of several new instrumental methods, and collecting/analyzing/organizing significant amounts of data. In addition, he will prepare and receive feedback on various visual representations of experimental results (i.e. preparing figures in a format appropriate for publication in a Chemistry journal). Prof. Dunham will work with Austin to prepare a scientific poster for presentation of this research at the 2016 Landmark Summer Research Conference, and for the 2017 Spring Annual Student Scholarship and Creative Endeavors Day.

Impact on faculty, campus community, and discipline. Austin's work on this project will contribute to the discipline of bioinorganic chemistry by characterizing model compounds between dirhodium complexes and DNA. This project will benefit Prof. Dunham by building upon work of several former research students (Donchez &

Kuperavage Summer 2011, Donchez Honors '12-'13, and Bartulovich Summer 2014, Honors 14-'15). Austin's results will help us better understand the types of complexes formed between dirhodium compounds and DNA. It is anticipated that his research will be part of a future publication of these compounds in a peer reviewed Chemistry journal. By presenting his research during the summer to the SOAR group, and as a poster at botht he 2016 Landmark Conference and at the Moravian Scholarship and Performance Day in April 2017, Austin's work will impact the campus community at Moravian by exposing others to interesting and complex nature of bioinorganic chemistry research.

Budget Items

- $500.00 to offset part of the costs for reagents required for synthesis and characterization of rhodium-DNA model compounds.

    - dirhodium trifluoroacetate, 1 g $ 259
    - 9-ethyl-guanine, 200 mg $ 320

    Total $ 579

- Remaining equipment and reagent expenses will be covered by the Department of Chemistry.

Dirhodium trifluoroacetate is a commercial starting material required for the synthesis of dirhodium complexes. It is a consumable reagent so there are no standard supplies of this compound available at Moravian.

The DNA model compound, 9-ethyl-guanine, is a commercially available compound that that resembles the DNA base deoxyguanosine (dG) found in DNA. This is a consumable reagent that is not available at Moravian.

SOAR Student Statement of Purpose – Summer 2016

Austin Mates

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Biochemistry Major

Moravian College Class of 2018

Project Title: Synthesis of Rhodium-DNA Model Complexes

Mentor: Dr. Stephen Dunham

Requesting On-Campus Housing

To say that I am enthusiastic to start doing real scientific research with the Student Opportunities for Academic Research program would be an understatement. I have always held a passion for the sciences, and I have a found a particular fervor to study biochemistry. While it is certainly necessary for me to learn about biochemistry from a classroom, I believe the SOAR program can further my understanding of biochemistry in a way that the classroom cannot. Unlike normal classwork I will be working directly with my mentor, Dr. Stephen Dunham on a project that I believe holds a lot of promise.

The basic premise of the project is the research of DNA-binding rhodium compounds. These compounds, when bound to double-stranded DNA, can form DNA cross-linkage. This linkage prevents the cell from copying its DNA, thus terminating the cell's life cycle. The ability to selectively kill cells via DNA-binding rhodium compounds can result in anti-tumor properties. Such compounds are quite desirable for the advancement of chemotherapy. It's obvious that such research holds serious implications for the future of chemotherapeutic treatments, I would be honored contributing to such an interesting topic of research. My mentor and I will be building off research done by past alumni who previously participated in the SOAR program. I am determined to continue the research with the kind of respect and reverence deserving of past graduates of Moravian College. By furthering their research I personally hope to gain some of the skills I'll need for when I'm working in laboratories in the future. Working in the laboratory for the SOAR program will be a stark contrast to work in classroom lab, I believe that such an experience will acclimate me to real career-based lab work.

I am certain that the Student Opportunities for Academic Research program will elevate my abilities and take me to the next level of my scientific ambitions. If I ever want to thrive in my own laboratory I need to experience real genuine lab work. Working with Dr. Stephen Dunham I hope that we will produce compelling, thought provoking results. This program will display the kind of zeal that I have for biochemistry while also building up practical skills I'll need for my professional career. Taking part in Student Opportunities for Academic Research program is an opportunity that I cannot let slip by me, I truly believe that this program will make my summer of 2016 meaningful.